Nano consortium concludes five years of scientific advances and collaboration

By Kelly Lenox

In 2010, NIEHS established a consortium of research centers to study the health effects of engineered nanomaterials for five years. As the project came to a close, consortium researchers gathered for a final meeting May 6-7 at Research Triangle Institute (RTI) International in Research Triangle Park, North Carolina, to share their scientific advances and discuss the challenges ahead.

Sri Nadadur, Ph.D., program director for the NIEHS Nanotechnology Environmental Health and Safety program, described the consortium's threefold research agenda. "We wanted researchers to address cellular and molecular level activity, then transfer those findings to animal studies," Nadadur explained. "And we wanted to take those observations and develop predictive modeling for risk assessment."

According to Nadadur, groundbreaking consortium research has been featured at diverse national and international scientific meetings, including the Society of Toxicology and the American Chemical Society. (Photo courtesy of Steve McCaw)

With more than 20 grantees, including eight research centers and several individual researchers, the consortium structure provided a means to share results and discuss challenges, Nadadur said. As a way to focus research, all grantees studied silver nanoparticles and multiwalled carbon nanotubes provided by NIEHS. In addition, researchers chose various other nanomaterials to study, including metal oxides, silica oxide, silver nanowires, carbon 60, and quantum dots.

Strategic, groundbreaking research

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., welcomed researchers. "The nano environmental health research program has become an important component in three strategic goals of the NIEHS strategic plan," she said.

Hernan Navarro, Ph.D., above, and Tim Fennell, Ph.D., not shown, are both with RTI International, which hosted the event. "NIEHS is grateful for the work they put in to make this meeting a success," Nadadur said.

Engineered nanomaterials (ENMs) are synthetic particles with any external dimension between 1 and 100 nanometers. They are at the forefront of a number of advances in medicine, technology, and consumer products, and until recently, little was known about their health effects.

Two days of research presentations, posters, and discussions revealed that consortium researchers have made significant inroads toward understanding the mechanisms of physiological responses to nanoparticle exposures, from rates of cellular uptake to inflammatory and cytotoxic responses.

Researchers also explored how those responses could be moderated by the size, charge, coating, and surface chemistry of the particles. "Two centers clearly demonstrated, at the cellular and animal levels, how physical and chemical properties influence cellular response," said Nadadur, who reviewed the highlights of the consortium results (see sidebar). "The consortium achievements in addressing the goals of nano environmental health are greater than any one individual effort," he added.

Insights to guide future designs

According to Nadadur, one of the NIEHS goals for the consortium was to make advances that would help guide the design of the next generation of nanomaterials. That goal was met, as evidenced by findings shared by several presenters.

For example, the team at the University of California, Los Angeles Center for Nanobiology and Predictive Toxicology explored whether there were unique nanoscale characteristics that contributed to hazards in the lung. Andre Nel, Ph.D, described their discovery that the effects of zinc oxide were less toxic when some of the zinc oxide particle's surface was coated with iron in a controlled manner.

The center at the University of California, Davis also studied respiratory effects. Kent Pinkerton, Ph.D., discussed his team's findings on how the surface coating of nanoparticles influenced the effects of exposure. "If we can work toward modifying the ways in which nanomaterials are synthesized, while maintaining their marvelous properties, I think we can find ways to create materials that are less toxic," he said.

"The consortium is the first coordinated nano program to integrate research findings across cellular, molecular, and organ levels of organization," Birnbaum noted in her welcome. "The ultimate goal of the program is to develop computational models to predict potential human health risks."

Results lead to next steps

By the end of 2014, more than 200 papers on consortium research had been published, and scores more are in review or preparation stages. NIEHS is using the results of this project to design the next one.

"To continue to build on the success and the scientific knowledge gained from this consortium, plans have been initiated for issuing new funding opportunity announcements," said Birnbaum. "Please stay tuned." Nadadur said announcements would be made in the near future.

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"We've set the stage for pushing the ball forward for how people can … produce tools that can be used in risk assessment," said Justin Teeguarden, Ph.D., left, from the Pacific Northwest National Laboratory (PNNL). Gunter Oberdorster, D.V.M., Ph.D., right, from the University of Rochester, serves on the consortium's external advisory committee. (Photo courtesy of Steve McCaw)

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Brian Thrall, Ph.D., of PNNL, discussed the protein coating, or corona, that formed on nanoparticles. "The method of [particle] synthesis can very much influence the surface crystals," he said, noting that nanosilver with a gold core produced a very different pattern of surface crystal than particles with a silver core. (Photo courtesy of Steve McCaw)

Highlights of consortium research

- Evaluated toxicity of 30 ENMs, including metals and metal oxides, with varying size, shape, and surface charge.
- Studied ways that ENMs are broken down and the effects of differences.
- Produced comprehensive biological response profiles of:
  - Silver nanoparticles with varied size and surface coatings.
  - Multiwalled carbon nanotubes with three different aspect ratios.
- Studied multiple routes of exposure, including inhalation, oral, and IV.
- Revealed characteristics of particle absorption, distribution, metabolism, and excretion, as well as toxicokinetics.
- Evaluated the role of genetic and disease susceptibility.
- For silver, developed *in vitro* sedimentation, dissolution, dispersion, and dosimetry modeling.

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Sally Tinkle, Ph.D., from the Science and Technology Policy Institute, is an external advisory committee member and a former NIEHS senior science advisor. "We were not going to move the field forward unless we tried to move in the direction of risk assessment," she said, referring to the predictive modeling component and the models presented at the meeting. "This is a proud moment for me, and I thank every one of you." (Photo courtesy of Steve McCaw)

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During a break, from left, Rick Woychik, Ph.D., deputy director of NIEHS, spoke with Elaine Faustman, Ph.D., and Terry Kavanagh, Ph.D., both of the University of Washington, and Terry Gordon, Ph.D., of New York University. Gordon said being part of the consortium advanced his team's research by providing access to the expertise and processes of other consortium members. (Photo courtesy of Kelly Lenox)

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From left, Jamie Bonner, Ph.D., of North Carolina State University; Jared Brown, Ph.D., of the University of Colorado; and Salik Hussain, D.V.M., Ph.D., from NIEHS, caught up during the poster session. Brown collaborated with the RTI center, which presented evidence that the placenta prevented transfer of nanomaterials to the fetus in pregnant rodents. (Photo courtesy of Steve McCaw)

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Ingrid Bergin, V.M.D., left, and Jessica Axson, Ph.D., both from the University of Michigan, listened during one of the lively discussion sessions during which researchers challenged assumptions and shared insights. (Photo courtesy of Steve McCaw)

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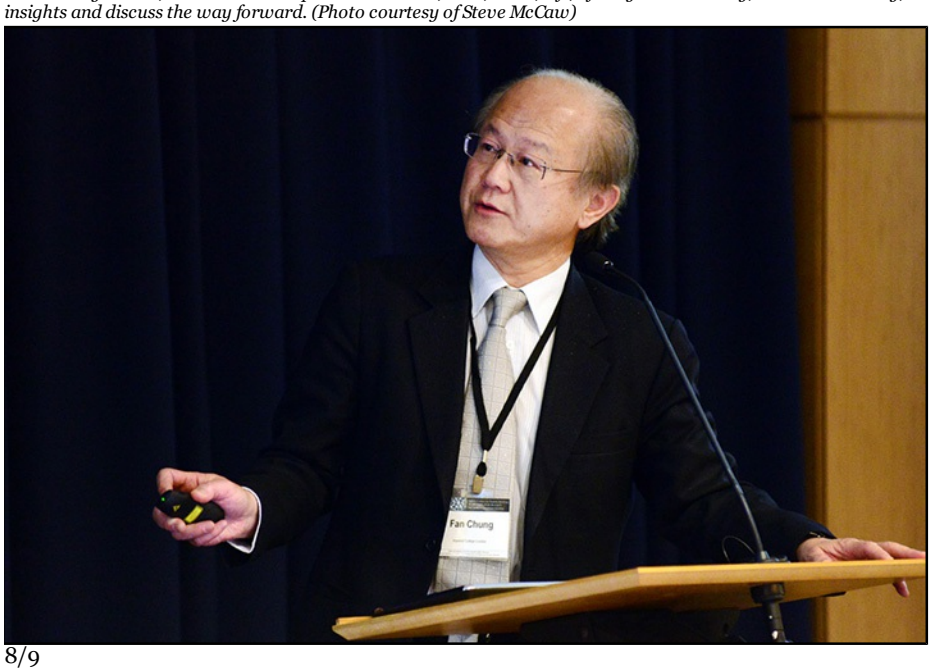
Even during breaks, scientists like Stephan Schwander, M.D., Ph.D., left, of Rutgers University, and Teresa Tetley, Ph.D., of Imperial College London, found time to continue to share insights and discuss the way forward. (Photo courtesy of Steve McCaw)



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Kian Fan Chung, M.D., D.Sc., of Imperial College London, discussed how health effects varied based on the shape of nanomaterials. For example, his team found that the inflammatory effect of exposure to silver nanowires was delayed compared with silver nanospheres. (Photo courtesy of Steve McCaw)

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Nadadur, who designed and implemented the consortium project, pondered the advances made and the number of questions that still need to be answered in the interest of public health. (Photo courtesy of Steve McCaw)

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